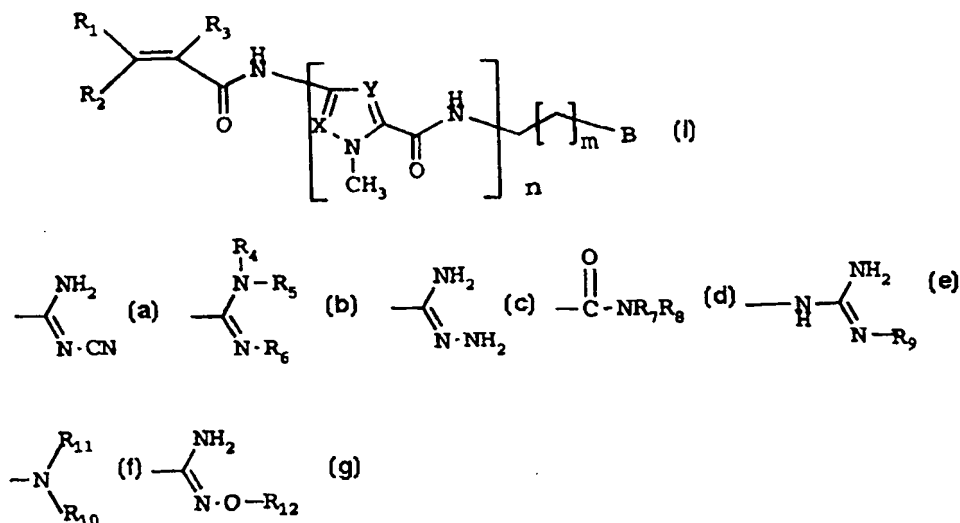




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07D 403/14, A61K 31/415		(11) International Publication Number: WO 99/50265
A1		(43) International Publication Date: 7 October 1999 (07.10.99)
(21) International Application Number: PCT/EP99/01822 (22) International Filing Date: 17 March 1999 (17.03.99) (30) Priority Data: 9806689.7 27 March 1998 (27.03.98) GB (71) Applicant (for all designated States except US): PHARMACIA & UPIOHN S.P.A. [IT/IT]; Via Robert Koch, 1.2, I-20152 Milan (IT). (72) Inventors; and (75) Inventors/Applicants (for US only): COZZI, Paolo [IT/IT]; Via Zanella, 48/5, I-20133 Milan (IT). BARALDI, Pier, Giovanni [IT/IT]; Via Tulipani, 73, I-44100 Ferrara (IT). BERIA, Italo [IT/IT]; Via G. Matteotti, 39, I-45030 Vil- lamarzana (IT). CALDARELLI, Marina [IT/IT]; Via Be- senzanica, 9, I-20147 Milan (IT). CAPOLONGO, Laura [IT/IT]; Via P. Rembrandt, 11, I-20147 Milan (IT). RO- MAGNOLI, Romeo [IT/IT]; Via Bologna, 291, I-44100 Ferrara (IT).		(81) Designated States: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>

(54) Title: ACRYLOYL DERIVATIVES ANALOGOUS TO DISTAMYCIN, PROCESS FOR PREPARING THEM, AND THEIR USE AS ANTITUMOR AGENTS



(57) Abstract

Compounds which are acryloyl substituted distamycin derivatives of formula (I) wherein: n is 2, 3 or 4; m is 1 or 2; X and Y are the same or different and are selected, independently for each heterocyclic ring of the polyetherocyclic chain, from N and CH; R₁ and R₂, which are the same or different, are selected from hydrogen, halogen, and C₁-C₄ alkyl; R₃ is hydrogen or halogen; B is selected from (a), (b), (c), (d), (e), (f), (g) and -C≡N; wherein R₄, R₅, R₆, R₇, R₈, R₁₀, R₁₁, and R₁₂ are, independently from each other, hydrogen or C₁-C₄ alkyl; and R₉ is hydrogen or hydroxy; or pharmaceutically acceptable salt thereof; provided that a) at least one of R₄, R₅ and R₆ is alkyl; b) at least one of the heterocyclic rings within the polyetherocyclic chain is other than pyrrole; and c) X and Y are not both N for the same heterocyclic ring; are useful as antitumor agents.